REMARKS/ARGUMENTS

Claims 1, 3, 5-7, 11, 12 and 19 are pending in the above-captioned application. Claims 8-9, 13-17 have earlier been withdrawn from consideration.

Claim 1 has now been amended to more particularly point out that which Applicants consider to be their invention.

Upon entry of the above amendments, therefore claims 1, 3, 5-9, 11-17, 19 are pending. Claims 8-9, 13-17 are withdrawn. The amended claims are fully supported in the specification as originally filed. The amendments to the claims do not add new matter. Applicants respectfully request that the amendments be entered.

The following remarks, in conjunction with the above amendments, are believed to be fully response to the Office Action.

THE REJECTION UNDER 35 USC § 103 SHOULD BE WITHDRAWN

The application names join inventors. The subject matter of the various claims was commonly owned at the time the inventions covered therein were made.

Claims 1, 3, 5-7, 11-12 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger, US Patent 6,033,645 ("Unger").

As noted above, claim 1 has been amended to recite that the invention is directed to a method of enhancing product homogeneity in the administration of a gas-containing contrast agent to a subject by continuous infusion. The contrast agent is administered by continuous infusion over an infusion period of 5-60 minutes, and is delivered from the upper extremity of an essentially vertically positioned syringe and is admixed with a flushing medium prior to

administration to the subject. Basis for the amendment, specifying that product homogeneity is enhanced, is found on page 4, lines 9-13 of the specification.

The present invention has identified a solution to a problem associated with the administration of a gas-containing contrast agent to a subject by infusion. A problem with the continuous infusion of gas-containing diagnostic contrast agents arises from the tendency of gas-containing components to float, since this will lead to inhomogenities forming within vessels such as power-driven syringes which may be used to administer the contrast agent. This may, for example, lead to an increase in microbubble concentration in the upper part of such a vessel and/or to changes in size distribution occurring at various points within the vessel as larger microbubbles float more rapidly than smaller microbubbles. This problem increases with increased time of administration of the contrast agent. By combining delivering from the top of a vertically positioned syringe and admixing with a flush medium prior to administration to a patient, the segregation is minimized and enhanced product homogeneity is achieved. By using a syringe as the delivery reservoir and placing this in a vertical position, with the outlet pointing upwards, the effects of floatation separation is greatly reduced, as further explained in the specification on page 3 and 4. The admixing with a flushing medium further enhances the homogeneity of the contrast agent that is delivered to the patient, e.g. by reducing the residence time of the agent in connecting tubes etc. It is further preferred that the syringe is positioned so that the bulk flow direction of the gas-containing contrast agent during expulsion is the same as the direction of segregation of the dispersed gas-bubble phase, i.e. upwards, since this will assist in counteracting the formation of concentration gradients of the dispersed gas-bubbles during administration. The claimed invention hence provides a method of administration wherein enhanced product homogeneity is achieved.

Unger discloses ultrasound contrast agents and delivery of such to a patient. However, as outlined in our previous response, Unger mentions infusion of contrast agents but fails to teach administration by continuous infusion, i.e. non-interrupted administration of the contrast agent and simultaneous admixture with flushing medium over time. Unger

describes that diagnostic artifacts, such as shadowing, may be reduced by controlling the rate of administration of the contrast agent and/or by administering a flush such as normal saline after administration of the contrast agent. The contrast agent of Unger is typically administered over a period of 5 seconds (column 45, line 20), or up to a period of 50 seconds ((column 3, line 55), and any subsequent flush is typically administered over a period in the range 10 seconds to 10 minutes. To promote the transport of the contrast agent from the injection site into the bloodstream, a flush may be administered to push or wash the contrast agent into the bloodstream (page 70). The contrast agent is hence delivered over a very short period, while the flushing media may be administered over a longer period.

Unger does not provide a method of enhancing product homogeneity during administration by continuous infusion. Unger indicates in figure 2 that the contrast agent can be administered from a vertically positioned syringe, but there is no teaching in the specification that the syringe is placed in this position to avoid segregation. If using a three-way connector as indicated in Figure 2 of Unger to connect the flushing media and the contrast agent syringe, it would for practical reasons be easiest to place one delivery vessel horizontally and one vertically. As Unger has not described why the syringe with the contrast agent has been positioned vertically it seems incidental that it is the vessel with the contrast agent that has been placed in this position and not the vessel with the infusion media. As argued above, claim 1, and subsequent claims, are not obvious based on Unger, as this does not suggest the claimed method of enhancing product homogeneity in the administration of a gas-containing contrast agent.

Even though Unger indicates that the rate of administration can be optimized, there is not suggestion of how to avoid segregation problems in the administration tubings if increasing the administration period.

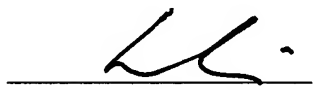
Thus, Applicants respectfully submit that the Examiner's rejection under 35 U.S.C. 103 (a) has been overcome and/or obviated and respectfully request that the rejections be withdrawn.

CONCLUSIONS

In view of the amendments and remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,



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